PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

CEFPODOXIME 40 mg/5 ml ADCO (powder for oral suspension)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml reconstituted suspension of CEFPODOXIME 40 mg/5 ml ADCO contains 40 mg of cefpodoxime as proxetil.

Preservative: Sodium benzoate 0,2 % *m/v*

Contains sugar: Sucrose 2,5 g per 5 ml

Contains sweetener: Aspartame* 0,02 g per 5 ml

*CONTAINS PHENYLALANINE

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension

An almost white to pale yellow coloured powder forming off-white to pale yellow suspension with a characteristic fruity odour upon reconstitution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CEFPODOXIME 40 mg/5 ml ADCO is indicated for use in the short-term treatment of infections due to susceptible micro-organisms:

- Upper and lower respiratory tract infections;
- otitis media;
- tonsillitis and pharyngitis;
- pneumonia.

4.2 Posology and method of administration

Posology

Each 5 ml of suspension contains 40 mg of cefpodoxime.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

The dosage depends on the weight of the child being treated. The average dose is 8 mg/kg/day administered in two doses at 12 hourly intervals. It must be taken with meals since an increase in gastric pH results in decreased bioavailability.
The following table may be used as a dosage guide:

Weight (kg)	**Dose**
Between 10 kg and 15 kg	5 ml (40 mg) every 12 hours
≥ 15 kg	10 ml (80 mg) every 12 hours

The use of CEFPODOXIME 40 mg/5 ml ADCO in children under one year of age is currently not indicated since insufficient clinical data is available at present (see section 4.3).

Special populations

Elderly

Where renal function is normal, it is not necessary to adjust the dose.

Renal insufficiency in adults and children

When the creatinine clearance is above 40 mL/min, it is not necessary to adjust the dose. For values below 40 mL/min, the daily dosage regimen should be reduced by half and administered as a single daily dose for values 10 mL/min to 39 mL/min, every second day for values below 10 mL/min and after each dialysis session for haemodialysis patients.

Method of administration

For oral administration.
Shake the bottle before use.
See section 6.6

4.3 Contraindications

CEFPODOXIME 40 mg/5 ml ADCO is contraindicated in:

- Hypersensitivity to cephalosporin antibiotics or to any other ingredient in CEFPODOXIME 40 mg/5 ml ADCO (see sections 4.4 and 6.1).
- CEFPODOXIME 40 mg/5 ml ADCO must not be given to children with phenylketonuria,

since the formulation contains aspartame (20 mg/5 ml).

- Safety in pregnancy and lactation has not been established.
- Patients with a previous history of immediate type hypersensitivity to cephalosporins.
- Children below 1 year of age (see sections 4.2 and 4.4)

4.4 Special warnings and precautions for use

Anaphylactic reactions

Preliminary enquiry as to an allergic diathesis and particularly hypersensitivity to beta-lactam antibiotics should precede treatment with CEFPODOXIME 40 mg/5 ml ADCO. The use of CEFPODOXIME 40 mg/5 ml ADCO is strictly contraindicated in subjects with a previous history of immediate type hypersensitivity to cephalosporins (see section 4.3). CEFPODOXIME 40 mg/5 ml ADCO should be used with extreme caution in patients sensitive to penicillin and other beta-lactam antibiotics as cross-allergy may develop. Strict medical supervision is required throughout the treatment. Hypersensitivity reactions (anaphylaxis) observed with CEFPODOXIME 40 mg/5 ml ADCO can be serious and occasionally fatal. Treatment should be stopped immediately, should an allergic reaction occur. Caution is also necessary in patients with a history of allergy (see section 4.3).

Clostridium difficile – associated disease

Diarrhoea, particularly if severe and/or persistent, occurring during treatment or initial weeks following treatment with CEFPODOXIME 40 mg/5 ml ADCO may be symptomatic of *Clostridium difficile* associated disease, the most severe form of which is pseudomembranous colitis. The diagnosis of this rare but possibly fatal condition should be confirmed by colonoscopy and/or histology. Screening of faeces for this pathogen, and its cytotoxin is the best way to diagnose *Clostridium difficile* associated disease. This occurrence requires immediate cessation of administration and treatment with appropriate specific antibiotic therapy such as vancomycin or metronidazole given orally when the colitis does not improve or when it is severe. *Clostridium difficile*-associated disease can be favoured by faecal stasis. Treatment should be discontinued if symptoms suggestive of pseudomembranous colitis arise. Mild cases of pseudomembranous colitis may respond to discontinuance of CEFPODOXIME 40 mg/5 ml ADCO. Pseudomembranous colitis may occur even after CEFPODOXIME 40 mg/5 ml ADCO is discontinued.

Renal impairment

CEFPODOXIME 40 mg/5 ml ADCO should be given with caution to patients with renal

impairment as it may result in increased blood levels and toxicity. Dosage reduction may be necessary. Changes in renal function have been observed with antibiotics of the same class as CEFPODOXIME 40 mg/5 ml ADCO, particularly when given concurrently with potentially nephrotoxic agents such as aminoglycosides and/or potent diuretics. Renal and haematological status should be monitored especially during prolonged high dose therapy. CEFPODOXIME 40 mg/5 ml ADCO may interfere with Jaffè method of measuring creatinine concentrations and may produce falsely high values.

Excipients

Contains 2,5 g of sucrose per dose. This should be taken into account in patients with diabetes mellitus.

Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take CEFPODOXIME 40 mg/5 ml ADCO.

CEFPODOXIME 40 mg/5 ml ADCO contains aspartame. Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. One of the major hydrolysis products is phenylalanine. Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age (see sections 4.2 and 4.3).

4.5 Interaction with other medicines and other forms of interaction

The bioavailability of CEFPODOXIME 40 mg/5 ml ADCO is increased if the product is administered during meals (acid pH).

- There is a risk of cross-sensitivity between cephalosporins and penicillins.
- The renal excretion of cefpodoxime, as contained in CEFPODOXIME 40 mg/5 ml ADCO, is delayed by probenecid.
- Absorption of cefpodoxime, as contained in CEFPODOXIME 40 mg/5 ml ADCO, is decreased by antacids or histamine H_2-receptor antagonists such as ranitidine.
- There may be antagonism between CEFPODOXIME 40 mg/5 ml ADCO and bacteriostatic antibacterials.
- Cephalosporins, such as CEFPODOXIME 40 mg/5 ml ADCO, in high doses frequently give a positive response to the antiglobulin (AGT) test although haemolytic anaemia may occur.
- Urinary glucose testing with non-specific reducing agents may yield a false-positive

reaction in patients treated with CEFPODOXIME 40 mg/5 ml ADCO. A false positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with copper sulphate test tablets, but not with tests based on enzymatic glucose oxidase reactions

- Concurrent use with anticoagulants; warfarin, may increase the risk of bleeding.
- Acute renal tubular necrosis has followed excessive dosage and has also been associated with use in older patients and those with pre-existing renal impairment, or when used with nephrotic medicines such as aminoglycosides.
- CEFPODOXIME 40 mg/5 ml ADCO reduces the contraceptive effect of oestrogens.

4.6 Fertility, pregnancy and lactation

The safety of CEFPODOXIME 40 mg/5 ml ADCO in pregnancy and lactation has not been established (see section 4.2).

Pregnancy

Safety of CEFPODOXIME 40 mg/5 ml ADCO in pregnant women has not been established, it is therefore advisable not to administer CEFPODOXIME 40 mg/5 ml ADCO during pregnancy (see section 4.3).

Breastfeeding

Since CEFPODOXIME 40 mg/5 ml ADCO is excreted in human breast milk, either breastfeeding or treatment of the mother should be discontinued in mothers who are breastfeeding their infants (see section 4.3).

Fertility

There is no available data on fertility.

4.7. Effects on ability to drive and use machines

Since adverse reactions such as dizziness have been reported in patients receiving CEFPODOXIME 40 mg/5 ml ADCO, patients should not drive, use machinery or perform any tasks that require concentration until they are certain that CEFPODOXIME 40 mg/5 ml ADCO does not adversely affect their ability to do so (see section 4.8).

4.8 Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Infections and infestations	Multiplication of non-sensitive micro-organisms, oral and vaginal candidiasis, superinfection		
Blood and the lymphatic system disorders		Hypoprothrombinaemia, haemolytic anaemia	Agranulocytosis, eosinophilia, leucopenia, neutropenia, reduction in haemoglobin, thrombocytosis, thrombocytopenia
Immune system disorders		Anaphylactic reactions, e.g. angioedema, bronchospasm, malaise, serum sickness-like	
Nervous system disorders	Headache	Seizures	Asthenia, dizziness and paraesthesia

Ear and labyrinth disorders		Hearing loss	Tinnitus
Gastrointestinal disorders	Abdominal pains, diarrhoea, flatulence, vomiting	Diarrhoea may sometimes be a symptom of enterocolitis, which may, in some cases, be accompanied by blood in stools	
Hepatobiliary disorders		Cholestatic jaundice, hepatitis	
Skin and subcutaneous tissue disorders		Bullous eruptions, cutaneous eruptions, erythema multiforme, Stevens-Johnson syndrome, skin rashes, pruritus, purpura, urticaria	
Renal and urinary disorders		Renal dysfunction	
Investigations			Increase of ASAT, ALAT, alkaline phosphatase, blood urea, creatinine

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

Treatment

Treatment should be symptomatic and supportive.

In cases of overdosage, particularly in patients with renal insufficiency, there is a risk of reversible encephalopathy for several cephalosporins (see section 4.8).

Convulsions have also been reported with very high doses especially in patients with renal impairment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 20.1.1 Broad and medium spectrum antibiotics

Pharmacotherapeutic group:

ATC code: Other beta-lactam antibacterials

ATC code: J01DD13

Mechanism of action

Cefpodoxime proxetil is a semi synthetic beta-lactam antibiotic belonging to the third generation oral cephalosporin group. Cefpodoxime proxetil is the prodrug of the bactericidal antibiotic cefpodoxime. Cefpodoxime possesses *in-vitro* bactericidal activity against a broad spectrum of Gram positive and Gram negative bacteria. *In-vitro* sensitivity does not necessarily imply *in-vivo* efficacy. Therefore sensitivity tests must be performed.

Cefpodoxime is stable in the presence of the majority of beta-lactamases. The mechanism of action is bactericidal through inhibition of bacterial cell wall biosynthesis enhanced by a high affinity for proteins at the cytoplasmic membrane.

The following organisms are not sensitive: Group D streptococci, Methicillin-resistant staphylococci (*S. aureus* and *S. epidermidis*), *Staphylococcus saprophyticus*, *Corynebacteri*, groups J and K, *Listeria monocytogenes*, *Pseudomonas aeruginosa* and *Pseudomonas* spp., *Acinetobacter baumanii*, *Clostridium difficile*, *Bacteroides fragilis* and related species.

5.2 Pharmacokinetic properties

The bioavailability of cefpodoxime proxetil is increased when the product is administered with meals, or when there is a decrease in gastric pH. An increase in gastric pH results in decreased bioavailability.

Absorption

After oral administration, cefpodoxime proxetil is absorbed in the gastrointestinal tract and rapidly hydrolysed by non-specific esterases in the gastrointestinal wall to cefpodoxime, the active acid.

Distribution

After oral administration of a single 5 mg/kg dose (200 mg maximum) of cefpodoxime to subjects between 4 and 12 years of age, the maximum plasma concentration (C_{max}) is on average 2,6 mg/L. The time taken to reach the maximum concentration (T_{max}) is 2 to 4 hours. The average plasma concentrations observed 8 and 12 hours after administration (residual) are 0,39 mg/L and 0,08 mg/L respectively. Cefpodoxime proxetil diffuses well in lung parenchyma, bronchial mucosa, pleural fluid and tonsils.

Biotransformation

The main metabolite is cefpodoxime, resulting from the hydrolysis of cefpodoxime proxetil.

Elimination

The elimination half-life of cefpodoxime is 2,4 hours. Eighty percent (80 %) of unchanged cefpodoxime is excreted in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Aspartame*, banana flavour, carboxymethylcellulose sodium, colloidal anhydrous silica,

hydroxypropyl cellulose, maize starch, microcrystalline cellulose, sodium benzoate, yellow iron oxide (C.I. 77492), sucrose

6.2. Incompatabilities

None known

6.3. Shelf life

24 months

6.4. Special conditions for storage

Before reconstitution:

Store at or below 25 °C.

Protect from light and moisture.

Keep in original packaging until required for use.

After reconstitution:

Use within 10 days.

Store at 2 °C to 8 °C (in a refrigerator).

Shake before use.

6.5 Nature and contents of container

32,4 g or 64,8 g powder equivalent to 50 ml or 100 ml suspension respectively, upon reconstitution. Suspension is packed into a round, white translucent high-density polyethylene bottle and sealed with a white polypropylene child-resistant cap with a foil seal. The bottle is placed in an outer cardboard carton together with a patient information leaflet.

Not all pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

Remove the screw-cap by simultaneously pushing and turning it. Remove the foil seal and discard. A total of 27 ml of water is required to make up 54 ml of the suspension in the 75 ml bottle and a total of 54 ml of water is required to make up 108 ml of the suspension in the 150 ml bottle. Add water and shake vigorously to disperse all granules.

PROFESSIONAL INFORMATION

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road,
Erand Gardens,
Midrand, 1685
Customer Care:0860ADCOCK/ 232625

8. REGISTRATION NUMBER

42/20.1.1/0387

9. DATE OF FIRST AUTHORISATION

Date of registration: 19 April 2013

10. DATE OF REVISION OF TEXT

Date of the most recent amendment to the professional information as approved by the Authority: 16 September 2022

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